REMARKS

Claims 8-13 and 15-24 are in the application. New claims 15-24 serve to clarify the invention and do not contain new matter. The amendments presented above are believed to overcome the 35 U.S.C. 112, first and second paragraphs rejections. Reconsideration and withdraw are deemed proper.

A copy of the figures labeled Fig. 1 and Fig. 2 are attached in response to the Examiner's request.

Applicants submit that the specification of the application does reasonably provide guidance for the construction of the key components of the vaccine. The synthesis and production of glycopeptides claimed in the present invention can easily be reduced to practice by one of average skill in the art. In fact, various procedures to synthesize and produce glycopeptides is detailed in the literature. Glycopeptides may be coupled to carrier molecules using standard techniques known to those of average skill in the art. Furthermore, administration of the cancer vaccine via subcutaneous, intra dermal, intra venal, intra rectal, intra peritoneal and trans mucosal, for example, is well known to those of average skill in the art. Various formulations, pharmaceutical compositions and medicinal applications of glycopeptides as tumor vaccines against MUC1 positive tumors are expected to be covered by the application and hence are not further detailed.

The Office action rejected claims 8-13 under 35 U.S.C. 102(b) as being anticipated by Hanisch et al., Cancer Res., 1995, Vol. 55(18):4036-40, abstract ("Hansich") or Taylor-Papadimitriou et al., WO/05142, May 17, 1990, claims 1-4 ("Taylor-Papadimitriou"). Applicants respectfully traverse.

At the time of filing, is was generally known that the APDTRP region of MUC1 is the main epitope for monoclonal antibodies generated in mice, as shown by a series of results from immunizations of mice followed by generation of monoclonal antibodies and their characterization. This was why the APDTRP region was named the immunodominant region of MUC1 by the scientific community which led to the common acceptance and belief that the threonine in this immunodominant region can not be glycosylated since this would prevent peptide specific antibody binding to this region. The present invention shows **unexpectedly** that this is not the case. Contrary to the state of the art, the present invention demonstrates that glycosylation of the threonine in the immunodominant region enhances the immunogenicity of MUC1 peptides dramatically as was evident from the significant enhancement in binding or the enablement of binding of a series tumor relevant antibodies to glycopeptides glycosylated at the PDTRP region compared to those not glycosylated at the immunodominant region. The dramatically increased immunogenicity of the glycosylated immunodominant region is not observed with short glycopeptides. Neither Hanisch nor Taylor-Papadimitriou teach or disclose such glycopeptides. Both references will be further discussed in detail below.

Applicants submit that neither Hanisch nor Taylor-Papadimitriou discloses the peptides of the invention. The Office action states that "Hanisch et al taught a MUC1 glycosylated amino acid sequence that is glycosylated by GalNAc1 (using an oligosaccharide) that is less than 20 amino acids in length, thereby anticipating the claim." (p. 5, Paper 12). Applicants respectfully disagree.

Hanisch describes a monoclonal antibody which recognizes a disaccharide linked to the exact position of the threonine of the MUC1 sequence VTSA. The VTSA-glycosylated peptide disclosed by Hanisch is not the peptide of the present invention. The VSTA peptide is outside the immunodominant region of MUC1. In contrast, the peptides of the present invention have to be glycosylated at the threonine of the PDTR region (immunodominant region). The present invention demonstrates that the glycosylation of the threonine of the immunodominant region is crucial for the increased immunogenicity defined by the antibody binding specificities. As shown in example 1 of the specification, glycosylations at the other 4 potential sites of the tandem repeat including the VTSA region play no role in the effect of increased immunogenicity. Furthermore, the present invention describes glycopeptides of at least 20 amino acids with increased immunogenicity in the immunodominant region. Thus, a MUC1 glycoslyated amino acid sequence that is less than 20 amino acids in length **does not** anticipate the claims of the present invention.

The Office action further states that "Taylor-Papadimitriou et al taught an amino acid sequence that is glycosylated by GalNAc that is less than 20 amino acids in length (see claims 1-4 especially), thereby anticipating the claim." (p. 5, Paper 12). Again, applicants respectfully disagree.

Taylor-Papadimitriou describes polypeptides having sequences corresponding to an antigenic epitope on human polymorphic epithelial mucin (hPEM). Specifically, Taylor-Papadimitriou claims peptide and glycopeptides with the sequence $\{X\}_x\{(A)_mPDTRP(A)_n\}_y\{X\}_z$ which contain only a partial sequence of the sequence necessary for increased immunogenicity claimed in the present invention. The Taylor-Papadimitriou peptides, exemplified by pentapeptide PDTRP, hexapeptide APDTRP, heptapeptide PDTRPA and octapeptide APDTRPA, are meant to mimic the antigenic epitope on hPEM. The present invention describes glycopeptides (of at least 20 amino acids) which include the immunodominant region and in addition, a larger sequence around this site comprising amino acids of the MUC1 sequence in order to achieve an increased immunogenicity. The Taylor-Papadimitriou sequences do not describe the present invention and focuses instead on the above mentioned penta to octapeptides flanked by one or more units of the same amino acid. Thus, Taylor-Papadimitriou does not anticipate or disclose the glycopeptides of the present invention.

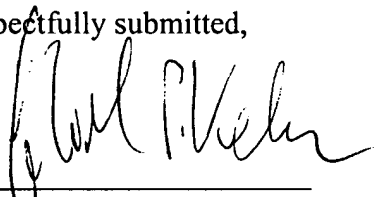
The Office action rejected claims 8-13 under 35 U.S.C. 102(e) as being unpatentable by McKenzie et al, US 5989552, filed April 9, 1997 ("McKenzie"). Applicants respectfully traverse.

McKenzie discloses fragments of MUC which may be chemically coupled to a carbohydrate polymer serving as a adjuvant. However, the MUC1 sequences which are disclosed are all not glycosylated at the potential glycosylation sites of the MUC1 tandem repeat including the immunodominant region. The glycosylation with the carbohydrate polymer is non-related to glycosylations claimed at the present application. Thus, McKenzie does not anticipate or disclose the glycopeptides of the present invention.

The Applicants wish to disclose PCT/GB88/00011 published as WO 88/05054 which was referred to in Taylor-Papadimitriou et al., WO/05142, May 17, 1990 already cited by the Examiner.

In view of the foregoing, reconsideration of the outstanding rejections, and the allowance of claims 8-13 and 15-24, are respectfully urged.

Respectfully submitted,



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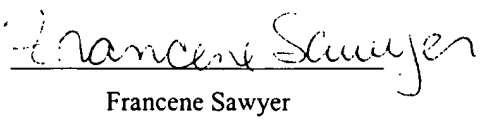
It is hereby certified that this is being mailed, as addressed above, on December 18, 2001.



Francene Sawyer

COMPARISON COPY OF CLAIM AMENDMENTS

8. A [tumor vaccine containing] synthetic peptide[s of a differing lenght which] compris[es]ing [glycosylating mostly but not exclusively] a sequence of the human epithelial mucin MUC1 [on threonine of the] wherein the peptide comprises the sequence, [contained immunodominant] PDTRPAP, the immunodominant sequence, [region] which is glycosylated at the threonine residue.

9. The [tumor vaccine] peptide of claim 8, wherein said synthetic peptide[s] ha[ve]s a length of at least about 20 amino acids.

10. The [tumor vaccine] peptide of claim 8, wherein [said] the glycosylation of the threonine of the PDTRPAP is [carried out by] a monosaccharide.

11. The [tumor vaccine] peptide of claim 8, wherein [said] the glycosylation of the threonine of the PDTRPAP is [carried out by] a α-N-acetylgalactosamine (GalNAc).

12. The [tumor vaccine] peptide of claim 8, wherein [said] the glycosylation of the threonine of the PDTRPAP is [carried out by] an [short-chain] oligosaccharide.

13. The [tumor vaccine] peptide of claim 8, wherein [said] the glycosylation of the threonine of the PDTRPAP is [carried out by] the disaccharide Galβ-1,[ ]3-GalNAcα.